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# Tracking Epileptogenesis Progressions with Layered Fuzzy K-means and K-medoid Clustering

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**Abstract**

This paper illustrates a method that identifies abnormal neurological events associated with acute brain injuries and seizures. The data is derived from intracortical electrodes that transmit EEG recordings that contain substantial amounts of noise. The output for the identification is specifically designed to be fed back into nan artificial intelligence unit the authors have designed that predict seizures in rats within 6 seconds of onset. This data will verify whether or not the prediction as accurate or not. The methodology set forth in this paper reflects the results of an ongoing research program that has investigated multiple techniques that have computational simplicity and are able to identify events with high precision. The paper presents our most recent in-house algorithm for seizure detection. The authors present this novel approach through the analysis of 3 channel EEG recordings from 3 rats that have 10 seizures each. The algorithm uses a Riemann sum analysis that compares the time to zero crossings with the absolute amplitude of the intervening signal. Herein, the authors present a system that incorporates clustering analysis using fuzzy K-means (FCM) and K-medoid clustering that identifies and separates artifact and normal states of animal with states seizure.

*Keywords:* Epileptogenesis, Fuzzy K-means, K-medoid Clustering

## 1. Introduction

The author's hypothesis is that in a domain of time versus amplitudinal strength in encephalograms of a rat during seizure, artifact remain stationary in continuous clustered segments while seizure activity should move. The basis for this is because the authors believed that artifact will be randomly distributed, specifically, the amplitude is lower with normal neural activity because its not coherent. Whereas the inverse should be true during seizure. The authors decided that the optimal means of challenging our hypothesis would be to represent the neurological activity in clusters with the x-axis representing change over time plotted against y-axis representing the amplitudinal strength. Choosing a means of clustering analytics lead us to applying the fuzzy c-means (FCM) algorithm and the k-medoid algorithm because they are often used in visualization for image segmentation, in our case the authors are performing encephalogram separation. Furthermore one knows that when noisy domain segmentation is required one typically modifies the FCM accordingly. Here, the authors performed minimal modification of the original algorithm once

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we clustered the signal on our in-house system. The resultant clustering and the movement of the clustering during epileptoid periods was remarkably distinct. This paper presents our methodology and the resultants. This paper is not a definitive resultant. However, we do believe that the dissemination of how we've identified a means to measure specific vector-based movement by tracking epileptogenesis with layered fuzzy K-means and k-medoid clustering.

## 2. Background

Epilepsy is a neurological disorder wherein clusters of neurons fire electrical signals abnormally that cause recurrent unprovoked seizures. Unfortunately, 30% of patients that suffer from epilepsy are not well controlled on medication. Only a small fraction of these can be helped by seizure surgery [1]. Therefore, it would be life changing to a large number of individuals if a system could be developed that would predict a seizure hours, minutes, or even seconds before its clinical onset. The challenge in this problem is that the dimensionality is huge; in the human brain there are approximately 100 billion neurons, each with about 1000 connections (synapses)[2]. Even in the rat brain it is estimated that there are approximately 200 million neurons [3], [4]. The connections are wired such that the problem is highly chaotic. In a certain class of seizures it would be helpful if they could be detected even a few seconds prior to the start of a seizure. The dimensionality of the problem can be significantly reduced, with only a small loss of information by recording electrical potentials at multiple points on the surface of the skull or, using depth electrodes, in the hippocampus (EEG). EEGs are accepted as one of the best means of evaluating neurocognitive functions [5]. EEG spike/seizure detection and prediction is made more complicated by the following: (1) For a single individual, no two seizures or even their EEG correlates are exactly alike, (2) seizures from different individuals vary significantly, (3) there is no single metric that consistently changes during all seizures, (4) correlation among channels can change significantly from one seizure to the next, and (5) even experts disagree as to what constitutes a seizure [6]. For the reasons listed above, rigid seizure detection rules do not produce good results [7], [8]. This is the focus of this paper: Improved epileptogenesis can be achieved when a narrower empirically identifiable means of determining when a seizure is occurring.

### *2.1. Recording Epileptogenesis*

Until 1992 most EEG analysis was based on analysis of brain slices [9] or anesthetized animals [10]. Kainic acid, a chemoconvulsant extracted from seaweed, was introduced to induce seizures in animals. This provided a major breakthrough particularly with the advent of monitoring the animals on video, but the equally significant subclinical seizures were impossible to detect with video monitoring alone. The field was further advanced through the development of a tethered recording system [11] in which multi-channel cortical and sub-cortical recordings could be obtained. The quality of recordings were further improved by incorporating a small pre-amplifier close to the skull, allowing for a significant increase in the signal to noise (S/N) ratio. Electrodes were placed stereotaxically in the hippocampus and secured in the skull [12], [13] Additional electrodes were placed directly on the dura. Dental cement was applied to hold the electrode pins together in a plastic cap that was later connected to the pre-amplifier. The pre-amplified signal was sent to an amplifier and from there to a computer for storage. Our facility has the capability of continuously monitoring up to 64 tethered or untethered rats. Untethered rats underwent video monitoring and the tethered rats underwent both video and EEG monitoring. This paper will discuss a novel means of illustrating, clustering and identifying artifact and seizure clusters using these animals.

### *2.2. Predicting Epileptogenesis*

Studies on clinical ictal activity are generally focused on mechanisms of epilepsy disease [14] , [15], most EEG studies deal with interictal epileptic activity rather than seizures. It is difficult to predict seizure occurrence due to the short time of recording and the artifacts generated by movements [16] Because they are considered as an indicator of the presence of epileptic seizures, and may actually precede a seizure (sentinel spike), the detection of these interictal, transient spikes which may be confused with artifact or noise is indeed a crucial element in the prediction of epileptic conditions. Work illustrating how interictal spikes can predict seizures by six seconds has been accepted in the community by using Deterministic Finite Automata [17], [18], [19]. Robustness of these predictive algorithms was attained by adding Spectral Analysis [20], [21], variant domains [22] and neurophysiological artificial intelligence [23]. The problem that our hypothesis focused on is that these interictal spikes do not always precede a seizure. It

follows that a more robust seizure detection mechanism can only be obtained when a substantially more objective means of having a machine identify when a seizure is occurring, or what is a seizure and what his not a seizure. This paper illustrates how the authors set up experiments to prove our hypothesis and how the results of our experiments provide a novel means to program a machine to identify seizures.

## 3. Background: Clustering

Clustering algorithms group similar patterns together, find application in pattern analysis, decision making and various machine learning problems. Clustering algorithms [24] essentially fall into either hierarchical or partitional clustering algorithms. Hierarchical algorithms produce a hierarchy of clusters. Agglomerative hierarchical clustering algorithms initially treat each pattern as a separate cluster and merge clusters recursively based on their distance from each other until a single cluster containing all the sought after patterns is obtained [25]. Our hypothesis is that if one were to cluster change of time for the x-axis and area under the curve then objects representing artifact will remain stationary in continuous clustered segments while objects representing seizure activity should move. Specifically, our objective is to partition a data set $\mathbf{X}$ into $c$ clusters where we assume that $c$ is known or it is a trial value of which partition results must be validated [26]. With classical sets we define a hard partition as a family of of subsets $\{A_i|1 \leq i \leq c \subset P(X)\}$ where $A_i$ contains all the data in $\mathbf{X}$, which must be disjoint, not empty nor contains all the data in $\mathbf{X}$. These three parameters in membership functions are, i) $V_{i=1}^{c}\mu A_i = 1$, ii) $\mu A_i \vee \mu A_j, 1 \leq i \neq j \leq c$ and iii) $0 < \mu A_i < 1, 1 \leq i \leq c$ where the function $\mu_{A_i}$ represents the subset $A_i$ which can be zero or one and in simplifying it we use $\mu_i$ rather than $\mu_{A_i}$. Our objective was to first use K-means and K-medoid algorithms which required hard partitioning and compare those results against Fuzzy K-means algorithm, requiring fuzzy partitioning, because for the system to work autonomously, a decision regarding supervised or unsupervised leaning will have to be made, i.e., comparing the hard and fuzzing partitioning at this stage is critical. To this end we defined hard and fuzzy partitioning in context to one another where in a hard partitioning space we let $\mathbf{X} = [x_1, x_1, ..., x_N]$ represent the finite set where $2 \leq c \leq N$ be an integer where the hard partitioning space for $\mathbf{X}$ is the set

$$\begin{aligned} M_{hc} &= \mathbf{U} \in \mathbf{R}^{N \times c} | \mu_{ik} \in 0, 1, \forall i, k; \sum_{k=1}^{c} \mu_{ik} = 1, \forall i, 0 \ldots \\ &< \sum_{k=1}^{c} \mu_{ik} < N, \forall k \end{aligned} \tag{1}$$

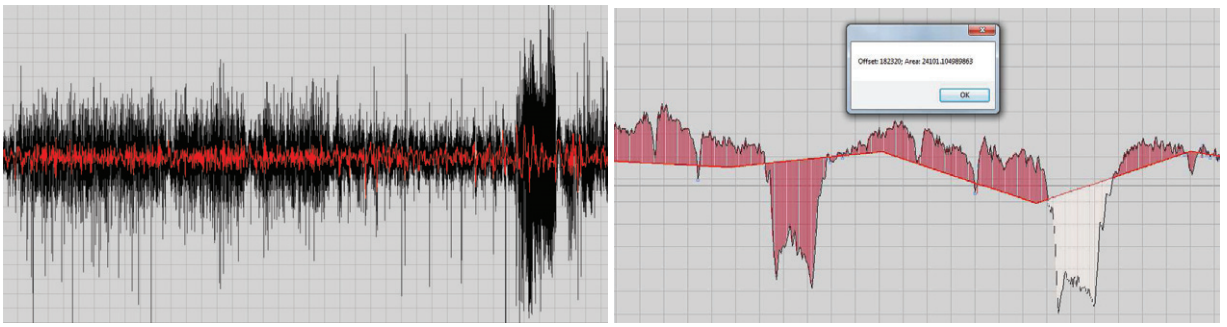
However, we need $\mu_{ik}$ to attain real values in [0,1] therefore we used Fuzzy partitioning as a generalization of hard partitioning where we let $\mathbf{X} = [x_1, x_1, ..., x_N]$ represent the finite set where $2 \leq c \leq N$ be an integer where the fuzzy partitioning space for $\mathbf{X}$ is the set

$$\begin{aligned} M_{fc} &= \mathbf{U} \in \mathbf{R}^{N \times c} | \mu_{ik} \in [0, 1], \forall i, k; \sum_{k=1}^{c} \mu_{ik} = 1, \forall i, 0 \ldots \\ &< \sum_{k=1}^{c} \mu_{ik} < N, \forall k \end{aligned} \tag{2}$$

where the $i$-th column of $\mathbf{U}$ contains values of the membership function of the $i$-th fuzzy subset of $\mathbf{X}$ and constrains the sum of each column to 1. This means that total membership of each $x_k$ in $\mathbf{X}$ equals one making the distribution of our memberships, artifact or seizure amongst the $c$ fuzzy subsets unconstrained and flexible in nature.

### *3.1. Hard Partitioning: K-means & K-medoid Algorithms*

The authors believe that the dimensionality problem can be solved by allowing partial membership. The Fuzzy set theory [27] provides useful concepts and tools to deal with imprecise information. Partial membership allows that the information about more complex situations, such as cover mixture or intermediate conditions, can be better




(a) (b)

Figure 1: Normal Signals for ICE. (a) The initial EEG signal: B4sz2, 195,000 samples @250Hz overlayed with mean spline averaged over 150 data samples (b) Export Utility: Export dialog offering several options for exporting processed data for further analysis using Matlab or Mathematica

represented and utilized [28]. The k-means and k-medoid algorithms divide the data set up into groups and attempt to accurately measure the distance between points in a cluster and a singular point deemed to be at the center of its cluster. The k-means algorithm partitions $n$ observations into $k$ clusters where each observation is a member of the cluster with the nearest mean. The k-medoid algorithm chooses data points as centers (medoids or exemplars). For our k-means algorithm the authors allocate each data point to one of $c$ clusters to minimize the within-cluster sum squares [29], [30] $\sum_{i-1}^{c} \sum_{k \in A_i} \|x_k - v_i\|2$ where $A_i$ is a set of objects in the $i$-th cluster and $v_i$ is the mean for the points inside of cluster $i$. The authors call $v_i$ the *clusterprototypes* where the cluster center is defines as $v_i = \frac{\sum_{k=1}^{N_i} x_k}{N_i}, x_k \in A_1$ where $N_i$ is the number of objects in $A_i$ K-medoid is a classical partitioning technique of clustering that clusters the data set of $N$ objects into $c$ clusters known a priori. Here the cluster centers are the nearest objects to the mean of data in one cluster $V = \{v_i \in X | 1 \leq i \leq c\}$

### *3.2. Fuzzy Partitioning: Fuzzy C-Means Algorithm*

The authors considered that becasue it is known that every algorithm that only uses inner products can implicitly be executed in the feature space that we could start with the original fuzzy c-means algorithm introduced by Dunn in 1974 [31], which he based on the minimization of an objective function called C-means functional. Dunn defines $V_i$ as the weighted mean of the data items belonging to a specific cluster, where the weights are the membership degrees. Hence the name "$c - means$". $J(X : U, V) = \sum_{i-1}^{c} \sum_{k \in A_i}^{N} (\mu_{ik})^m \|x_k - v_i\|^2$ where $V = [v_1, v_2, ..., v_c], v_i \in R^n$. Considering that $m$ is the weighting exponent on each fuzzy membership and determines the amount of fuzziness of the resulting classification. For clustering in a manner that artifact and seizure will be separated from the grey area, it seemed a viable option to also include FCM because the FCM objective function is minimized when high membership values are assigned to pixels whose intensities are close to the centroid of its particular class, and low membership values are assigned when the point is far from the centroid [32].

## 4. Experiments

### *4.1. Overview*

EEG data derived from the itracortical electrodes placed stereotaxically in the hippocampus and dura of the rats is amplified and recorded in ASCI files 24/7. When the animal has a seizure the authors sliced the ASCII file 2 minutes before the seizure occurred and ended it 60 seconds after what experts agree was the end of the seizure event.. Dental cement was applied to hold the electrode pins together in a plastic cap that was later connected to the pre-amplifier. Manipulation of the ASCI files was performed by Mathematica 8, MatLab and our custom-developed digital signal processing (DSP) software using .NET 4.0 and C#. In the next step the authors imported the ASCI data using our DSP which then applied visualizations of the signal by projecting the sample points making up the signal. Once created we projected a mean spline through the signal see (see Figure 1a), where it calculated the area of the curves under and above the mean spline (see Figure 1b. Then we exported the absolute values of the calculated areas into segmented and

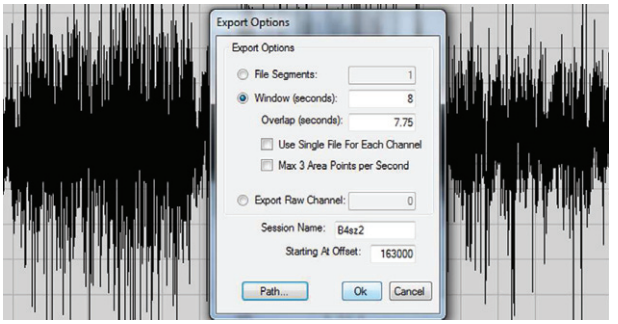
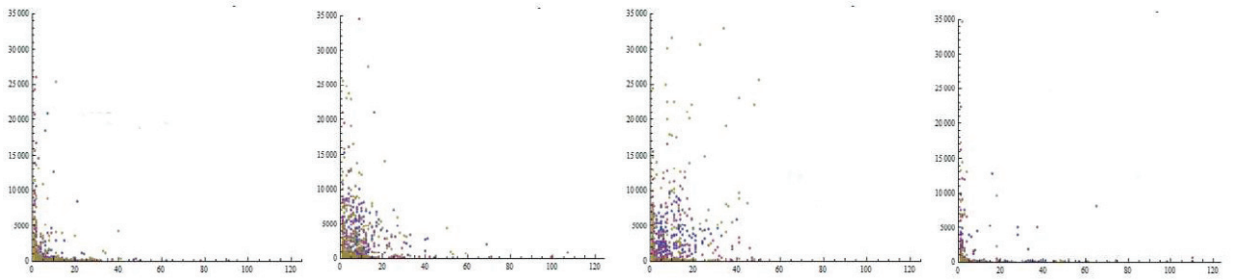



Figure 2: *Export Utility*: Export dialog offering several options for exporting processed data for further analysis using Matlab or Mathematica



(a) (b) (c) (d)

Figure 3: *B4sz2*:Three channels of EEG data, starting from 163,000 through 194,999; the area of seizure activity. (a) Depicts "normal" activity leading up to episode. (b) Relates to massive upward movement.(c) Brief movement to the right is observed, before movement drops back down toward (c) (left -lower corner).

overlapped time windows. The authors coded clustering for Mathematica and specific K-Means, K-medoid and fuzzy c-means in Matlab to automatically create animated plots showing clustering by change in time vs. area under/above (abs) the mean spline.

### *4.2. Data*

In this experiment the authors examined seizures of ten rat data files containing epileptic seizure activity recorded on three independent channels. It became apparent6, with the naked eye that a signature pattern of movement was becoming evident once the animals began to have their seizures. The concentrated regions all take place between offsets 160,00 and 170,000, and continued through the remaining data in the files totaling 2.33 minutes of data. the authors have, and still are continuing to experiment with how long the time windows used for exporting should be. At the time of this paper, a time window of eight seconds with a seven second overlap was determined to be adequate for analysis. The illustrations of clustered movement are based on this time window coupled with a mean spline averaged and interpolated for every one hundred fifty points over the entire signal.

### *4.3. Code*

## 5. Results

### *5.1. Graphical Context*

After running seizures of 10 rats through the system Figure 4 is representative of the cluster movements of all the rats. These four stages include the rest or normal state represented in the top left image. The rat is sleeping or eating and all is normal as the clusters indicate. However, after the interictal spike, the top right hand image shows a traveling of the centroid up along the y-axis. NO rat had a traveling cluster in any other direction during this first stage which is remarkable. Then in the bottom left hand image one observes the clusters returning to the (0,0) position. Finally in the second half of the seizure the centroid move at an incredible speed towards the upper right hand side of the chart.

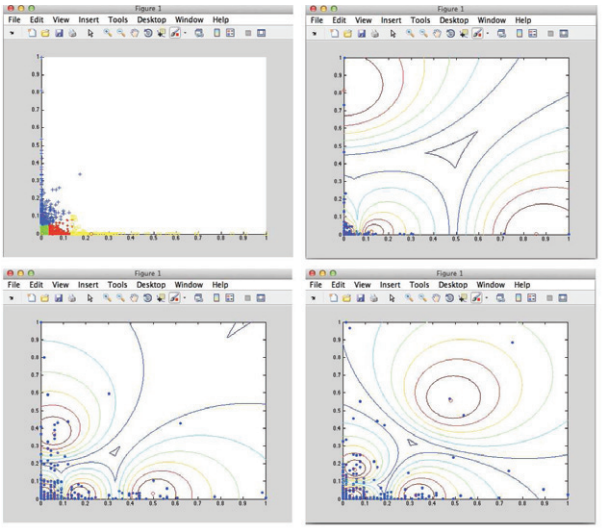


Figure 4: *Clustering*:Matlab renditions of b6z4's two stage seizure. Top left hand image is k-means showing normal state. Upper right hand image shows left hand cluster traveling upward. Bottom left hand image shows clusters returning back to the (0,0) position. the final, right hand image shows clusters jumping up towards the upper right hand side as the animal enters the second stage of the seizure..

## 6. Conclusion and Future Work

Our conclusion is that based off the animals tested and the continuous results justifying our hypothesis, that we can state that in a domain of time versus amplitudinal strength in encephalograms of a rat during seizure, artifact remain stationary in continuous clustered segments while seizure activity should move. However, for future work the authors have implanted intracortical electrodes into 20 new animals that will vein seizing in March, 2012. At this point we will record these seizures and rerun these experiments. The authors will also work on finding a better means to combine the seizures of many rats onto one graph and, if possible, determine a means to find a vector-driven mechanism to measure velocity and angles of seizures.

## 7. Acknowledgments

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